

## Periodic Fasting: A Strategy for Improving Cardiometabolic Parameters and Antioxidant Levels in Obesity

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### Abstract:

**Objective:** Obesity is associated with decreased antioxidant activity, such as Superoxide Dismutase (SOD), and due to metabolic switching processes, Periodic Fasting (PF) as a potential therapeutic approach must be further studied. The study aimed to analyze the effects of PF on cardiometabolic parameters, metabolic switches, and antioxidant levels.

**Material and Methods:** This was a quasi-experimental study conducted in Surabaya, East Java, Indonesia, consisting of the intervention (PFG) group, which received PF for 10 days, and the Control Group (CG), which had daily meals. The measurements of metabolic parameters, such as anthropometric parameters, fasting blood glucose (FBG), total cholesterol (TC),  $\beta$ -Hydroxybutyrate ( $\beta$ -HB), and antioxidant level, were taken pre and post-intervention.

**Results:** Thirty-six young adult men participated in this study. After 10 days, there was a significant improvement in most cardiometabolic parameters in the PFG group ( $p$ -value $<0.05$ ), including a reduction in FBG and TC ( $p$ -value $<0.05$ ). In the PFG group, the post-test mean  $\beta$ -HB level was significantly higher than the pre-test ( $21.48 \pm 8.86$  vs.  $15.63 \pm 3.71$ ,  $p$ -value $<0.05$ ), and the mean SOD level also increased ( $76.64 \pm 3.62$  vs.  $73.56 \pm 4.10$ ,  $p$ -value $<0.05$ ). There was a negative

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correlation between PF and the difference ( $\Delta$ ) in FBG ( $p=0.000$ ) and between post-test SOD, abdominal circumference (AC), and body weight (BW) ( $p=0.041$ ,  $p\text{-value}<0.05$ ).

**Conclusion:** The ability of PF to improve cardiometabolic parameters, including metabolic switch and antioxidant levels, makes it a feasible dietary intervention for obesity-related and associated health problems.

**Keywords:**  $\beta$ -Hydroxybutyrate, cardiometabolic parameters, metabolic switch, obesity, periodic fasting, superoxide dismutase

## Introduction

The rising obesity epidemic is one of the most crucial public health challenges worldwide. According to the World Obesity Atlas 2023, the number of overweight and obese individuals in 2020 was 2.6 billion (38% of the global population). It is estimated to rise to 4 billion by 2035 (50% of the worldwide population)<sup>1</sup>. Fat accumulation in obese and overweight individuals is associated with increased oxidative stress and decreased antioxidant activity<sup>2</sup>. Furthermore, obesity-related diseases, including diabetes, hepatic and renal dysfunction, cancer, asthma, infertility, and cardiovascular issues, are all associated with increased oxidative stress<sup>3</sup>.

In addition to obesity prevention and management, a therapeutic strategy for weight management, improving cardiometabolic parameters, and reducing oxidative stress is required. In this case, dietary modifications such as fasting are presumed to have a crucial impact, such as regulating lipid metabolism to reduce body mass and positively influence lipid profile parameters<sup>4,5</sup>. Superoxide dismutase (SOD) is a type of metalloenzyme that functions as an antioxidant against oxidative stress in the body and is thought to be an anti-aging enzyme<sup>6</sup>. According to Colak et al. (2020), obesity can cause a reduction in antioxidant enzymes like SOD<sup>2</sup>. This condition is similar to aging, which is characterized by declining SOD enzyme levels<sup>7</sup>. A decrease in this enzyme is directly related to the most

important biomarker of oxidative stress in individuals with metabolic syndrome and cardiovascular risk<sup>8</sup>.

Fasting may enhance antioxidant defenses and protect against lipid peroxidation due to the nuclear factor erythroid 2 (NFE2)-related factor 2 (Nrf2)-related antioxidant response<sup>4,9</sup>. Fasting can also alleviate oxidative stress by increasing ketone bodies due to metabolic switching processes<sup>4,10</sup>. In addition to its role as an alternative energy source, circulating ketone bodies, particularly  $\beta$ -Hydroxybutyrate ( $\beta$ -HB), have also been shown to alleviate oxidative stress by promoting mitochondrial biogenesis and mitophagy<sup>10</sup>. According to Klob et al. (2021), an increase in ketone bodies increases ketosis, which initially causes oxidative stress. This oxidative stress will have long-term advantages because it can trigger an adaptive response that activates Nrf2, sirtuins, AMPK, and the antioxidant gene SOD<sup>11</sup>.

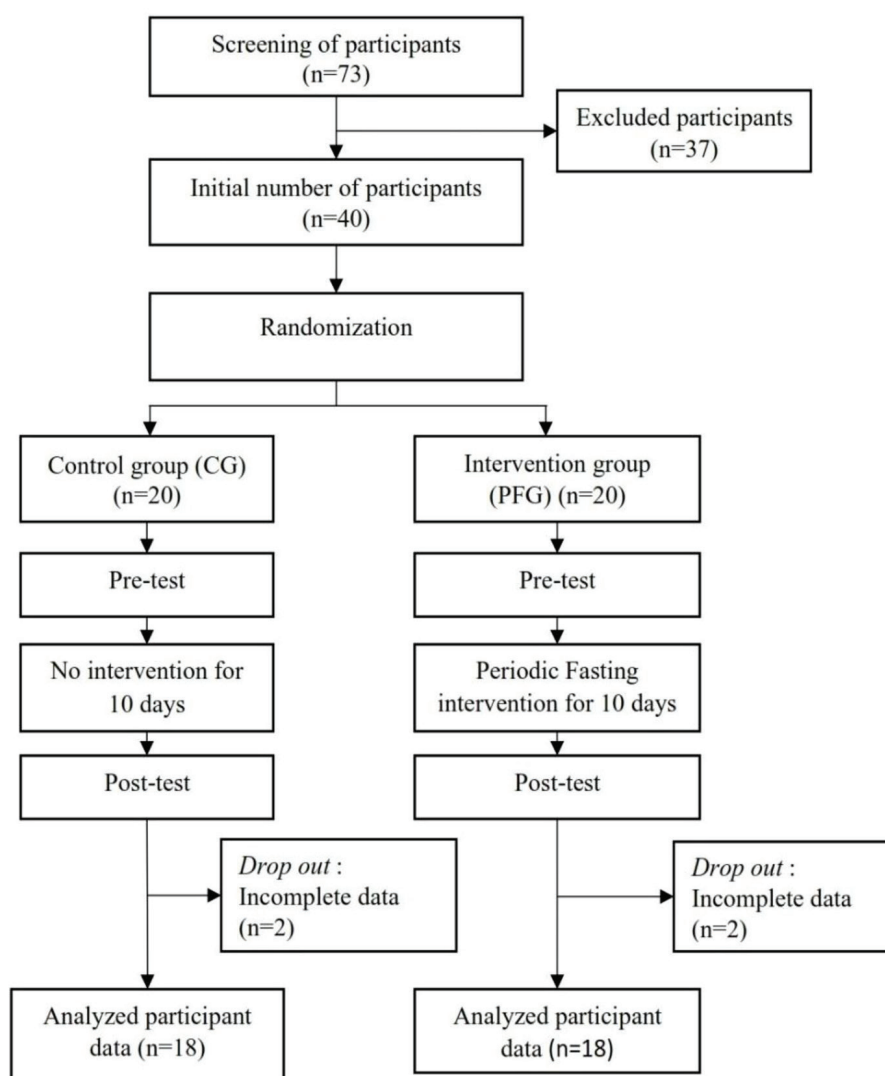
One type of fasting that might be interesting is periodic fasting (PF)<sup>12</sup>. PF defines intermittent fasting (IF) as fasting intervals ranging from 2 to 21 or more days, simulating diets<sup>13</sup>. A prior study found that blood redox status, mental and physical health, and associated cardiovascular and general risk factors can all be regulated by PF without focusing on a specific body mass index (BMI) range<sup>13,14</sup>. Previous studies have been carried out to determine the benefits of fasting for treating or preventing obesity and obesity-induced aging<sup>15,16</sup>. However, further

studies that can analyze the physiological and biological key mechanisms underlying the benefits of fasting, particularly in humans with obesity, are still needed. Based on this background, this study aimed to analyze the effects of PF on cardiometabolic parameters, including metabolic switches, by examining FBG, TC,  $\beta$ -HB, and SOD levels as antioxidants.

## Material and Methods

### Study design

This randomized, quasi-experimental, pre-test, and post-test group design was conducted on obese young male participants. This study consisted of 2 groups: the intervention group (PFG), which received PF for 10 days, and the control group (CG), which did not receive any therapy. Study data were taken twice during the pre-test and post-test. The study flowchart can be seen in Figure 1.



**Figure 1** Study flowchart

### Participants

This study population was young adult males with obesity. Participants were required to meet the inclusion criteria. Eligible participants with age >20 years, good health, a BMI  $\geq 25$  kg/m<sup>2</sup> according to the guidelines for Asians, and light-to-moderate physical activity (<600 MET or 600–3,000 MET) as measured by the Global Physical Activity Questionnaire (GPAQ) participated in this study<sup>17–21</sup>. Individuals with a history of diabetes mellitus, thyroid, parathyroid, heart disease, cancer, alcohol consumption, smoking, vegetarianism, veganism, daily use of acetylsalicylate drugs, use of hormonal medications, and currently enrolled in weight-loss programs were excluded<sup>22</sup>. The sample size in this study was calculated based on the sample size formula according to Chow et al (2018) with standard deviation and mean difference values referring to previous research<sup>13,23</sup>.

$$n = \frac{(z_{\alpha/2} + z_{\beta})^2 \times SD^2}{(x_1 - x_2)^2}$$

From this formula, the minimum sample for each group was 11. Of the 73 participants, only 40 met the criteria and were divided equally into 2 groups. After recruitment, participants were invited to a WhatsApp group and the physiology laboratory in Airlangga and Muhammadiyah Surabaya to conduct an examination.

### Ethical consideration

This study was conducted according to the principles of the Declaration of Helsinki. This study was registered by the Faculty of Medicine Ethics Committee, Airlangga University, Surabaya, Indonesia (No.157/EC/KEPK/FKUA/2022). Written informed consent was collected after the study protocol was explained to participants. Participants voluntarily participated in this study without any pressure.

### Fasting and diet methods

Participants in the PFG were asked to fast for 12 hours for 10 days (from 06.00 am to 06.00 pm). The PFG of study volunteers were only allowed to eat meals provided by the authors for 10 days<sup>12–14,24</sup>. Dietary regimen according to daily calorie requirements with a restriction of 500–800 kcal/day from the daily requirements<sup>24</sup>. No special regulations on the daily menu and fluid requirements were guaranteed to be at least 2 liters/day or 8 glasses. Daily urine conditions confirmed hydration status. The daily condition of participants, including food intake and any concerns about fasting, was observed. The CG and PFG groups were encouraged to comply with their current eating protocol, exercise, and physical activity throughout the study.

### Cardiometabolic parameters measurements

Cardiometabolic parameters in this study consisted of vital sign parameters and anthropometric parameters. Vital sign parameters included systolic blood pressure (SBP), diastolic blood pressure (DBP), and heart rate (HR). Blood pressure parameters were measured 3 times. SBP and DBP were measured on the non-dominant arm using an OMRON Digital Tensimeter (Omron Healthcare Manufacturing Vietnam Co., Ltd, Binh Duong, Vietnam), with a one-minute rest interval between readings. Examination of anthropometric parameters such as body weight (BW), body mass index (BMI), hip circumference (HC), abdominal circumference (AC), waist circumference (WC), and upper-arm circumference (UAC). Anthropometric parameters, such as BW and BH, were measured standing and reported to the nearest 0.5 kg using scales GEA ZT-120 (Zhongshan Camry Electronic Co., Ltd, Guangdong, China). Based on standards from Asia-Pacific, BMI was calculated by dividing body weight by height squared (Kg/m<sup>2</sup>) and was then categorized into multiple groups<sup>20</sup>. According to the WHO

protocol, HC was measured as the largest circumference at the buttocks, AC was taken midway between the inferior margin of the last rib and the crest of the ilium in a horizontal plane, and WC was measured at the smallest point between the highest point of the iliac crest and the bottom of the ribcage. Sometimes, the same measurement results were obtained for AC and WC. UAC was measured at the midpoint of the upper arm<sup>25,26</sup>. Fasting blood glucose (FBG), total cholesterol (TC), and uric acid (UA) levels were measured using a glucometer (Zhongshan CAMRY Electronic Co., Ltd, Jhunan Township, Taiwan).

#### Blood sampling and storage

Blood samples were collected twice (before and after treatment): one day before and on the eleventh day of the week, between 07.00 and 09.30 am Western Indonesia Time (WIB; UTC+7), before the subjects had breakfast. Before drawing blood, individuals were asked to sign an informed consent form. Expert medical personnel obtained blood samples from the antecubital veins of all the participants. As many as 3 ccs of blood were allowed to flow into the vacutainer and placed into a tube with ethylene diamine tetra acetic acid without additives.

#### Ketone bodies measurements

$\beta$ -HB levels in blood serum were measured twice: before and after treatment using the  $\beta$ -Hydroxybutyrate Assay Kit colorimetric tests (cat.no MAK041; Sigma; Spruce Street, Saint Louis, MO 63103, USA). During the initial stage, samples, reagents, and equipment were ready. Standard wells, test, and control samples (zero) were prepared on a pre-coated plate, and the solution was placed at the bottom of each. 50  $\mu$ l of the diluted standard was added to the standard well. 50  $\mu$ l of standard buffer diluent was added to the control well (zero), followed by 50  $\mu$ l of the diluted sample in the test well. A microplate shaker was

used to homogenize the samples. Following this stage, 50  $\mu$ l of Detection Reagent A was added to each well, re-homogenized, and incubated for 1 hour at 37 °C. Following washing, each well was filled with 100  $\mu$ l of the Detection Reagent B working solution, and it was then incubated at 37 °C for 45 minutes. After another washing cycle, 90  $\mu$ l of TMB substrate was added to each well, homogenized, and incubated for 10–20 minutes at 37 °C. After adding 50  $\mu$ l of stop solution to each well, the  $\beta$ -HB level was immediately measured at OD 450 nm.

#### Antioxidant measurement

SOD levels were measured in the participant's blood plasma using Total Superoxide Dismutase (TSOD) Activity Assay Kit (WST 1 Method) (Cat.no E-BC-K020-M; Elabscience; USA). Blood plasma was used to evaluate SOD levels. The samples were centrifuged for 10 minutes at 2,000 g, and the supernatant was collected for testing. The supernatant was then diluted with normal saline in various quantities. Each well received a total of 20  $\mu$ l of distilled water; the control well received 20  $\mu$ l of distilled water and 20  $\mu$ l of enzyme working solution; the blank control received 20  $\mu$ l of double distilled water and 20  $\mu$ l of enzyme diluent; and the sample well received 20  $\mu$ l of sample and 20  $\mu$ l of enzyme working solution. A 200  $\mu$ l substrate solution was mixed with a multi-channel pipettor into each well. The samples were incubated at 37 °C for 20 minutes, and the OD value was measured in each well using a wavelength of 450 nm with a microplate reader.

#### Statistical analysis

The Statistical Package for the Social Sciences (SPSS) version 25 statistical program for social science (SPSS, Inc., Chicago, IL, USA) was used to analyze the data gathered. Continuous data were expressed as mean $\pm$ S.D. The data normality was evaluated using the

Kolmogorov–Smirnov test; the differences between the pre-test and post-test were analyzed using the Paired T-Test and Wilcoxon; and group differences were determined using the independent t-test/Mann–Whitney test. The correlation between the variables was analyzed using Smart PLS<sup>27</sup>.

## Results

### Baseline characteristics of study participants

Out of 70 individuals, 40 participants who met the criteria were enrolled in the study. Thirty-six participants (90%) completed the study. Four participants dropped out of the study due to incomplete data. Out of the total participants, 18 were assigned to the CG group and 18 were assigned to the PFG group. Baseline participant characteristics can be seen in Table 1. Participants in the PFG and CG groups had a mean age of 20.61 ( $\pm 0.92$ ) and 20.89 ( $\pm 1.07$ ) years old, respectively. The Independent T-test ( $\pm$ ) and Mann–Whitney Test ( $\downarrow$ ) results showed no significant difference in baseline characteristics between the CG and PFG groups.

**Table 1** Baseline characteristics of participants in the control (CG) and periodic fasting (PFG) group

Characteristics	CG (n=18)	PFG (n=18)	p-value
Age (years)	20.89 ( $\pm 1.07$ )	20.61 ( $\pm 0.92$ )	0.43 <sup>‡</sup>
BW (kg)	88.47 ( $\pm 13.15$ )	82.94 ( $\pm 9.87$ )	0.16 <sup>‡</sup>
BH (m)	171.08 ( $\pm 7.07$ )	169.03 ( $\pm 6.57$ )	0.12 <sup>‡</sup>
BMI (kg/m <sup>2</sup> )	30.30 ( $\pm 4.73$ )	28.92 ( $\pm 2.09$ )	0.61 <sup>‡</sup>
SBP (mmHG)	125.56 ( $\pm 10.27$ )	121.00 ( $\pm 8.77$ )	0.12 <sup>‡</sup>
DBP (mmHG)	88.33 ( $\pm 8.57$ )	85.56 ( $\pm 7.84$ )	0.39 <sup>‡</sup>
HR (x/minute)	85.17 ( $\pm 12.76$ )	87.50 ( $\pm 8.84$ )	0.74 <sup>‡</sup>

BW=body weight, BH=body height, BMI=body mass index, SBP=systolic blood pressure, DBP=diastolic blood pressure, HR=heart rate, Data were reported as mean  $\pm$  standard deviation, The difference between the baseline characteristics of participants was analyzed using the Independent T-test when the data were normally distributed ( $\pm$ ) or the Mann–Whitney U-test when the data were not normally distributed ( $\downarrow$ )

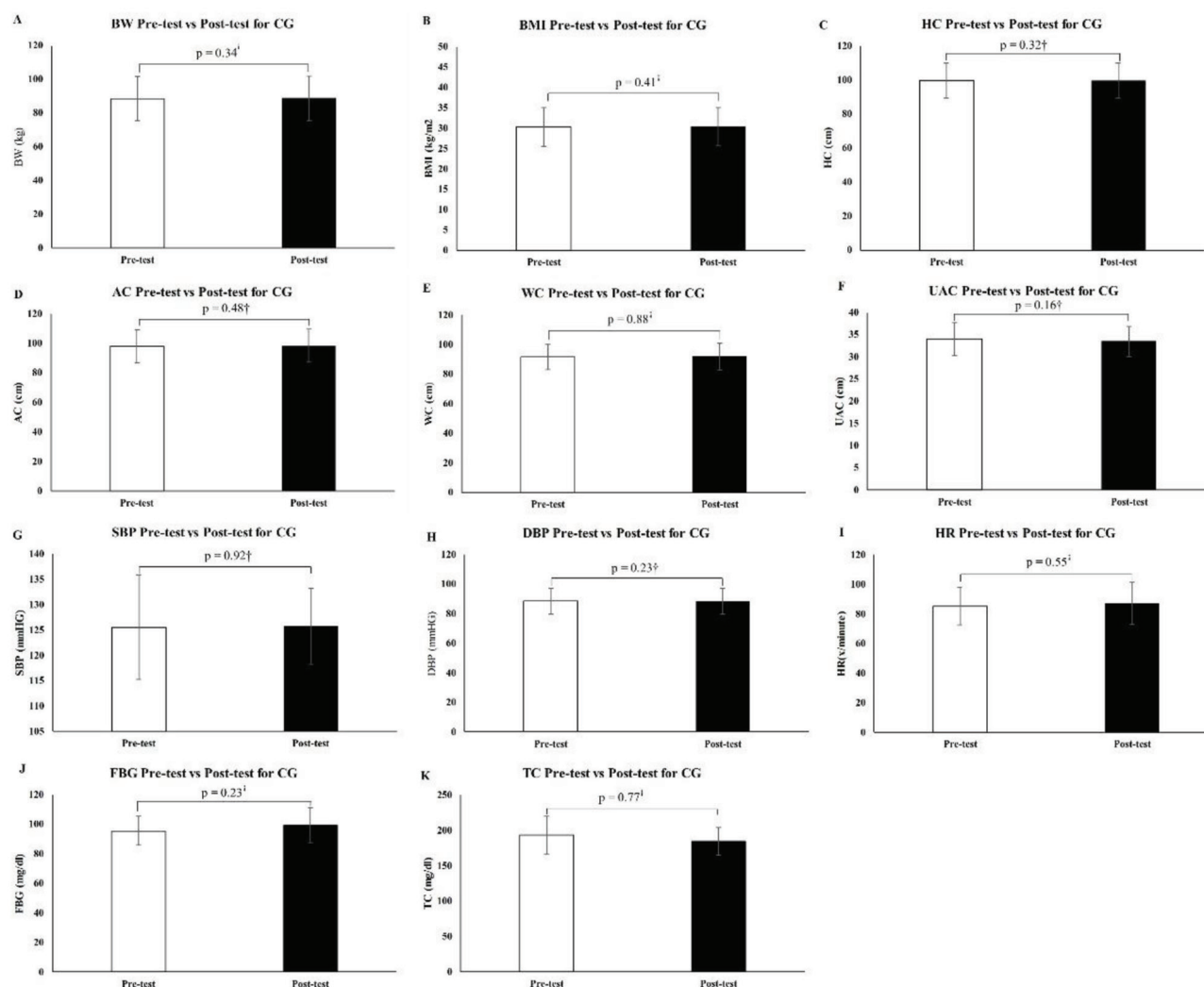
### Effects of PF on cardiometabolic parameters in the CG and PFG groups

This study analyzed the cardiometabolic parameters of participants (Figures 2 and 3). A comparison analysis of pre-test and post-test means was carried out to examine the impact of PF on cardiometabolic parameters in the CG and PFG groups. The Paired T-test results showed no significant difference in any of the pre-test and post-test cardiometabolic parameters in the CG group (all p-value $>0.05$ ) (Figure 2), while in PFG groups a significant difference was found in BW (p-value=0.00), BMI (p-value=0.00), AC (p-value=0.00), WC (p-value=0.00), SBP (p-value=0.01), FBG (p-value=0.00), and TC (p-value=0.00) (Figure 3). Statistical analysis also shows the significant differences in the change between pre-test and post-test in some parameters such as BW (p-value=0.00), BMI (p-value=0.00), AC (p-value=0.01), WC (p-value=0.02), and FBG (p-value=0.00) between the CG and PFG groups according to the Independent T-Test and Mann–Whitney test results. It was found that the post-test mean value of BW, BMI, AC, WC, SBP, FBG, and TC was lower than the pre-test mean value in the PFG group.

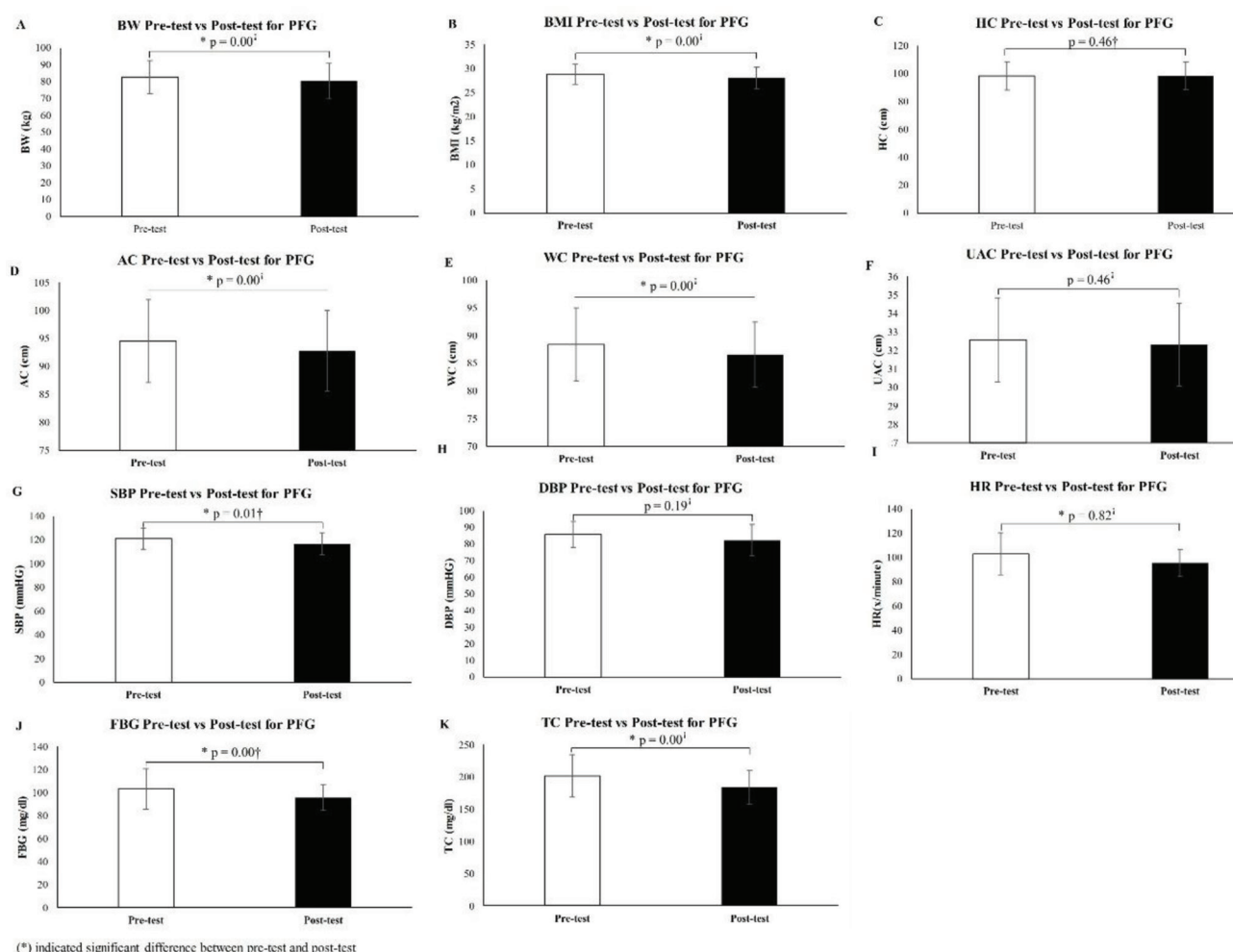
### Effects of PF on $\beta$ -Hydroxybutyrate ( $\beta$ -HB)

Figure 4 displays the results of  $\beta$ -HB levels in the pre-test and post-test in both groups. After 10 days of observation (post-test),  $\beta$ -HB levels in the CG group showed no significant differences (p-value=0.46) using the Wilcoxon Test. However, there was a significant difference in the PFG group (p-value=0.00) using the Wilcoxon Test. The post-test mean  $\beta$ -HB levels were significantly higher than the pre-test, with a value of 21.48 ( $\pm 8.86$ ) and 15.63 ( $\pm 3.71$ ), respectively, (p-value $<0.05$ ) in PFG. Nevertheless, using Mann–Whitney tests, this study indicates non-significant differences in  $\beta$ -HB changes between the CG and PFG groups (p-value=0.18).



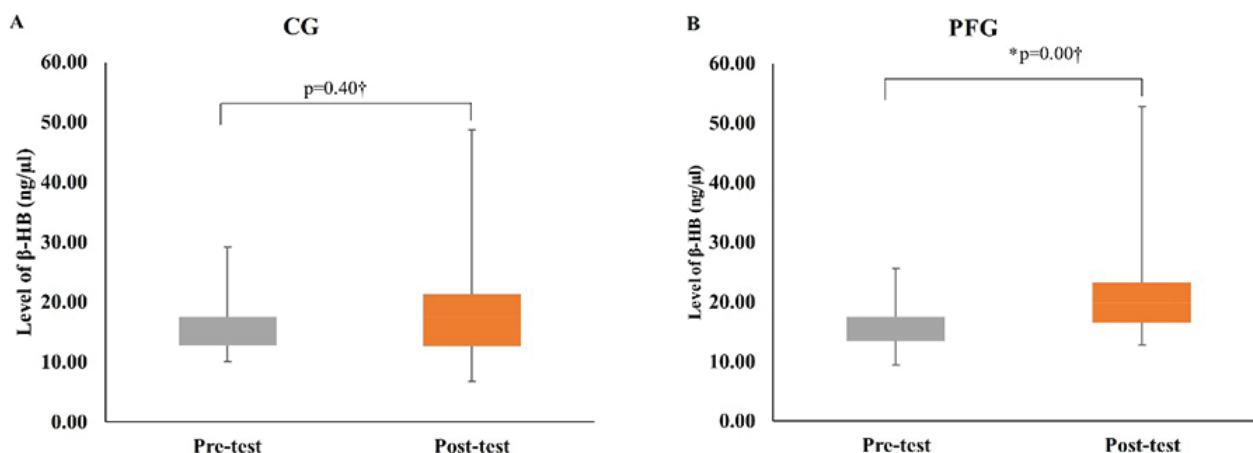


**Figure 2** Cardiometabolic characteristics in the control group (CG) after 10 days. A) Body weight (BW); B) Body mass index (BMI); C) Hip circumference (HC); D) Abdominal circumference (AC); E) Waist circumference (WC); F) Upper-arm circumference (UAC); G) Systolic blood pressure (SBP); H) Diastolic blood pressure (DBP); I) Heart rate (HR); J) Fasting blood glucose (FBG); K) Total cholesterol (TC). The analysis was determined based on the 10-day observation points before (pre-test) and after PF (post-test). The difference between pre-test and post-test data was analyzed using the Paired T-test when the data was normally distributed (<sup>†</sup>) or the Wilcoxon Test when the data was not normally distributed (<sup>†</sup>). Significant results are indicated by a superscript sign (\*)



**Figure 3** Cardiometabolic characteristics in the intervention group (PFG) after 10 days PF. Body weight (BW), Body height (BH), Body mass index (BMI), Hip circumference (HC), Abdominal circumference (AC), Waist circumference (WC), Upper-arm circumference (UAC), Systolic blood pressure (SBP), Diastolic blood pressure (DBP), Heart rate (HR), Fasting blood glucose (FBG), and Total cholesterol (TC). The analysis was determined based on the 10-day observation points before (pre-test) and after PF (post-test). The difference between pre-test and post-test data was analyzed using the Paired T-test or the Wilcoxon Test. The difference between pre-test and post-test data was analyzed using the Paired T-test when the data were normally distributed (<sup>1</sup>) or the Wilcoxon Test when the data were not normally distributed (<sup>†</sup>). Significant results are indicated by a superscript sign (\*).





(\*) indicated significant difference between pretest and posttest

**Figure 4** Effects of PF on  $\beta$ -HB after 10 days. A)  $\beta$ -HB in CG groups; B)  $\beta$ -HB in PFG groups. The difference between pre-test and post-test data was analyzed using the Wilcoxon Test because  $\beta$ -HB data were not normally distributed (<sup>†</sup>). Significant results are indicated by a superscript sign (\*)

### Effects of PF on SOD

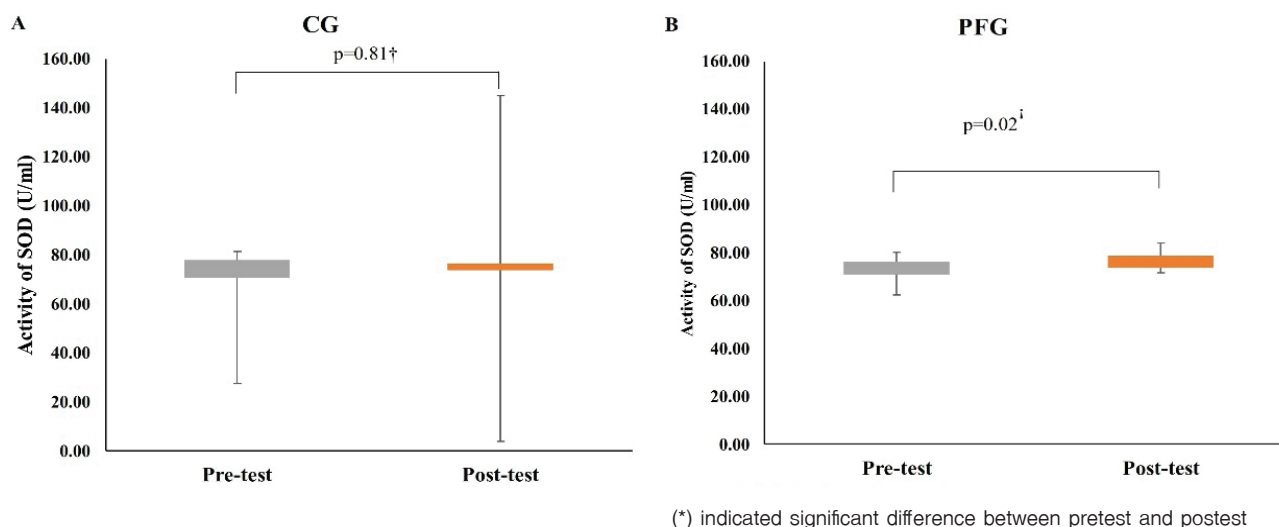
Figure 5 displays the results of SOD level in the pre-test and post-test in both groups. After 10 days of observation (post-test), using the Wilcoxon Test, SOD levels in the CG group showed no significant differences (p-value=0.81). However, there was a significant difference in the PFG group (p-value=0.02) using a Paired T-test. The mean SOD level in the PFG group was higher on the post-test ( $76.64 \pm 3.62$ ) compared to that on the pre-test ( $73.56 \pm 4.10$ ). Nevertheless, this study indicates non-significant differences in SOD changes ( $\Delta$ ) between the CG and PFG groups using Mann-Whitney tests (p-value=0.15).

### Analysis of the correlation between parameters

Figures 6A and 6B show the correlation between variables using path analysis. Figure 6A displays this path analysis to analyze the direct link between variables in post-test data for both groups (CG and PFG). The study

revealed that only the relationships between SOD and AC (p-value=0.041) and SOD and BW (p-value=0.026) were statistically significant. The original sample (O) correlation between SOD and AC was -0.170. These findings suggest a negative correlation between SOD and AC, with an increase of one unit of SOD projected to reduce AC by 0.17 units. The original sample (O) correlation between SOD and BW was -0.179. These findings show a negative correlation between SOD and BW, with an increase of one unit of SOD.

Only the correlation between PF and FBG was significant (p-value=0.000), according to the path analysis results on the different ( $\Delta$ ) parameters in Figure 6B. The original sample (O) correlation between PF and FBG was -0.434. These findings suggest a negative correlation between PF and FBG, with an increase of one unit of PF projected to reduce FBG by 0.43 units.



**Figure 5** Effects of PF on SOD after 10 days. A) SOD in CG groups; B) SOD in PFG groups. The difference between pre-test and post-test data was analyzed using the Paired T-test when normally distributed (<sup>i</sup>) or the Wilcoxon Test when not normally distributed (<sup>†</sup>). Significant results are indicated by a superscript sign (\*)

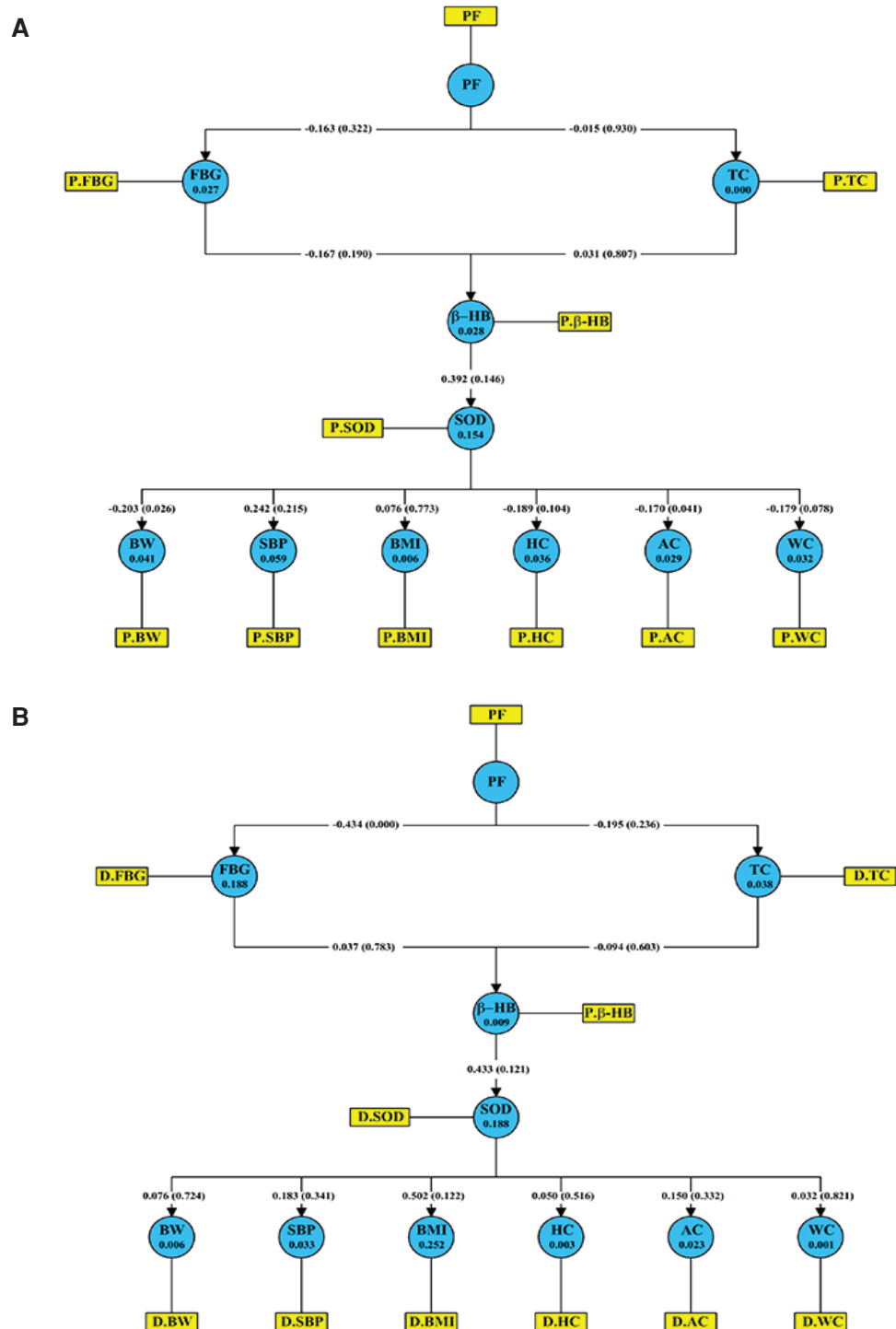
## Discussion

Ten days of PF can improve the cardiometabolic characteristics of individuals with a higher BMI. These conclusions are supported by significant changes in PFG (Figure 3). These findings are consistent with several studies suggesting that different IF techniques can boost weight loss and other anthropometric parameters, such as BMI, AC, and WC, and also enhance cardiometabolic health in overweight or obese individuals<sup>28-31</sup>. PF can improve anthropometric parameters by reducing visceral adipose tissue with weight loss<sup>32,33</sup>. By depleting glycogen from liver cells, fasting results in lipolysis and the generation of ketone bodies, reducing body fat<sup>34</sup>.

The finding of declining SBP levels in this study aligned with previous studies. PF can lower blood pressure due to increased parasympathetic activity from brain-derived neurotrophic factors (BDNF) and improved sensitivity to insulin and natriuretic peptides<sup>30</sup>. Since BDNF can boost acetylcholine production and release cholinergic

neurons, it has been shown in animal studies to promote parasympathetic activity. The vagus nerve releases acetylcholine to the sinoatrial node, which lowers the heart rate and regulates cardiac function<sup>30,35</sup>. Furthermore, the neurotransmitter causes the blood vessels to enlarge, which lowers blood pressure. IF enhances insulin sensitivity of muscle and liver cells and reduces IGF-1 production<sup>30,34</sup>.

According to this study, PF reduces FBG. These results support an earlier study that enhanced the effect of fasting on controlling glycemic levels<sup>30,31</sup>. After a 12-hour fast, the body begins to use fat cells' stored fatty acids to replace glucose in the metabolism, which raises insulin sensitivity. Depletion of liver glycogen stores occurs with a decline in insulin levels<sup>30</sup>. In line with the earlier study, IF significantly decreased the level of TC<sup>28-31</sup>. The breaking down of triglycerides (TGs) deposited in adipose tissue as fat after meals for an energy source for cells may cause this decreased level of TC<sup>30</sup>.



**Figure 6** A) Path Analysis using Partial Least Squares (PLS) in post-test results; B) Path Analysis using Partial Least Squares (PLS) in the changes of results

A fascinating finding in this study was the possible enhancement of  $\beta$ -HB levels (Figure 4) and a significant decrease in blood glucose levels by PF in the PFG group (Figure 3). These findings suggested that PF induced a metabolic switch, according to theory. These findings support the study of Gureev et al. (2019), which found that diet modification might increase and sustain the levels of circulating ketone bodies, particularly  $\beta$ -HB<sup>10</sup>. A metabolic switch brought on by intermittent fasting lowers FBG, which causes the liver to convert fat into ketones and ketone bodies by breaking down triglycerides into fatty acids and glycerol<sup>12,36</sup>. The increased ketone bodies in this study were presumed to serve as an alternative energy source and lower oxidative stress by encouraging mitophagy and mitochondrial biogenesis<sup>10</sup>.

PF can lower FBG and improve  $\beta$ -HB. However, path analysis does not reveal a significant direct or indirect link between variables. Only the correlation between PF and FBG is significant when delta values between the 2 groups are compared (Figure 6B). These findings show that the PF in this study was minimal in causing the metabolic switch. In theory, the metabolic switch happens between 12 and 36 hours after food consumption stops and is highly reliant on a variety of factors such as liver glycogen at the start of the fast, insulin resistance, the kind and duration of fasting, and the precise measurement time<sup>12</sup>.

Additionally, this study demonstrated that PF was able to increase SOD enzyme levels (Figure 5) significantly. The results are in line with other studies on various types of IF, which showed that consistent IF practice elevated SOD activity and improved cognitive performance<sup>37-39</sup>. Studies conducted on humans and animals have demonstrated that PF was able to increase SOD activity by interacting with the Nrf2-related antioxidant response<sup>9,40</sup>. Furthermore, a substantial rise in  $\beta$ -HB and a substantial fall in BW might potentially trigger a surge in SOD via activation of Nrf-2 due to the consequent oxidative stress<sup>11,39</sup>.

The path analysis of post-test results shows that SOD has a substantial negative correlation with AC and BW (Figure 6A). In other words, an increase in SOD will result in a decrease in AC and BW. SOD is a vital enzyme that protects mitochondria from oxidative damage. This study's findings support the concept that persons undergoing weight loss experience a considerable increase in SOD activity<sup>39</sup>. Aside from reducing body weight, further studies indicate that SOD is significant in reducing adipose tissue weight, insulin resistance, and overcoming adipose tissue malfunction caused by hypoxia. Thus, these parameters would be very interesting to study further.

Although PF can enhance cardiometabolic parameters, boosting metabolic switch and SOD, there does not appear to be a strong relationship between the variables. This could be due to some shortcomings in this study. The small sample size was the one limitation of this study. The PF duration used in this study is still within the minimum range for inducing a metabolic switch. As a result, further studies must be conducted with larger sample sizes and longer study periods in order to obtain optimal results. The metabolic transition typically occurs between 12 and 36 hours after fasting; hence, studies on various fasting durations are also required to determine the best fasting method<sup>12,14</sup>.

Obesity is linked to increased rates of oxidative stress. ROS production and the antioxidant activity against damage in this study remains limited to one enzymatic antioxidant, SOD<sup>8</sup>. Since SOD is an essential antioxidant defense mechanism against oxidative stress and its activity may be a valuable marker for determining the oxidative state in people undergoing weight loss, further study is necessary<sup>39</sup>. In addition, further study is required to analyze other ROS productions and the antioxidant activity parameters accompanied by other metabolic parameters, including blood energy substrate (triglyceride, free fatty acid, glycerol, and high-density lipoprotein), hormones and metabolism-related adipokines, body compositions,

energy use, and substrate oxidation<sup>29</sup>. However, this study provides the initial evidence that by increasing the metabolic switch and SOD enzymes, PF can elevate cardiometabolic parameters in young adult males with obesity.

## Conclusion

PF can improve cardiometabolic parameters, including metabolic switch and antioxidant levels in young adult men with obesity. These results show that PF has the potential to become a dietary intervention for the management, prevention, and treatment of obesity-related diseases.

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## Conflict of interest

The authors declare no conflict of interest.

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